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ORIGINAL REPORT

Psychosocial Factors and Survival of Young Women With Breast Cancer: A Population-Based Prospective Cohort Study

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ABSTRACT

Purpose
Most women with early-stage breast cancer believe that psychosocial factors are an important influence over whether their cancer will recur. Studies of the issue have produced conflicting results.

Patients and Methods
A population-based sample of 708 Australian women diagnosed before age 60 years with nonmetastatic breast cancer was observed for a median of 8.2 years. Depression and anxiety, coping style, and social support were assessed at a median of 11 months after diagnosis. Hazard ratios for distant disease-free survival (DDFS) and overall survival (OS) associated with psychosocial factors were estimated separately using Cox proportional hazards survival models, with and without adjustment for known prognostic factors.

Results
Distant recurrence occurred in 209 (33%) of 638 assessable patients, and 170 (24%) of 708 patients died during the follow-up period. There were no statistically significant associations between any of the measured psychosocial factors and DDFS or OS from the adjusted analyses. From unadjusted analyses, associations between greater anxious preoccupation and poorer DDFS and OS were observed ($P = .02$). These associations were no longer evident after adjustment for established prognostic factors; greater anxious preoccupation was associated with younger age at diagnosis ($P = .03$), higher tumor grade ($P = .02$), and greater number of involved axillary nodes ($P = .008$).

Conclusion
The findings do not support the measured psychosocial factors being an important influence on breast cancer outcomes. Interventions for adverse psychosocial factors are warranted to improve quality of life but should not be expected to improve survival.

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INTRODUCTION

The belief that cancer outcomes might be related to psychological factors dates back to around 200 AD when Galen hypothesized that melancholic women were predisposed to breast cancer.[1] In recent decades, there has been much interest in psychoneuroimmunologic pathways as the possible mediator of any such effect.[2-4] Whether psychosocial factors do actually influence outcomes in early-stage breast cancer remains controversial despite a relatively large body of literature on the subject.[5] The factors sometimes, but inconsistently, associated with survival in previous studies are depression and emotional repression (worse survival) and denial, minimization of illness, and social support (better survival).[5] As highlighted by others, though, problems with study methodology[6,7] and interpretation of results[8] have contributed to the lack of clarity around whether such associations are real or artifactual. Most studies have reported statistically significant associations between at least one psychosocial variable and disease outcome,[5] but many of these are likely to have been false-positive results owing to multiple significance testing.[8]

Yet the question remains an important one. A diagnosis of breast cancer is frequently associated with psychological distress,[9,10] and most patients believe that their psychosocial response to their breast cancer diagnosis affects their prognosis.[11] If this were true, appropriate psychosocial interventions might improve survival after breast cancer. Conversely, if no such effect exists, women's concerns could be allayed and this burden of responsibility lifted.

This study was initiated to examine the potential impact of anxiety and depression, coping style, and social support on distant disease-free survival

(DDFS) and overall survival (OS) for women diagnosed with locoregional invasive breast cancer.

PATIENTS AND METHODS

The Australian Breast Cancer Family Study (ABCFS) is a population-based, case-control-family study of the genetic, environmental, and lifestyle factors associated with breast cancer and is the Australian component of the National Institutes of Health Breast Cancer Family Registry.[12] It commenced in 1992 and recruited incident cases of primary breast cancer in women living in Sydney or Melbourne, Australia. Recruitment was organized via the respective state cancer registries (reporting of cancer to these registries is a legislative requirement). Given the particular interest of the ABCFS in genetic factors, younger age groups were oversampled. Approval for the study was obtained from the ethics committees of the University of Melbourne and the Cancer Councils of Victoria and New South Wales, Australia. All patients provided written informed consent for participation in the study. Overall participation by patients with breast cancer in the ABCFS was 69%. Nonparticipation was due to attrition by death (2%), refusal by the attending doctor (8%), refusal by the case patient (16%), nonresponse by the attending doctor (1%), nonresponse by the patient (1%), or inability to locate the patient (2%). Details of recruitment strategy, participation, and baseline data collection methods have previously been described.[13]

To be eligible for the current study of psychosocial factors, women had to be diagnosed with nonmetastatic breast cancer before the age of 60 years, have no previous history of invasive cancer (apart from nonmelanocytic skin cancer), be able to speak and read English, and be residing in Melbourne at the time of diagnosis.

Data Collection

Epidemiologic and psychosocial questionnaires. At study entry, in a face-to-face interview, participants were administered epidemiologic questionnaires, as previously described.[13] The median time between diagnosis and interview was 11 months (range, 2 to 42 months; interquartile range, 8 to 16 months). At the same time, participants were given a self-administered psychosocial questionnaire that included the Hospital Anxiety and Depression Scale (HADS), Mental Adjustment to Cancer (MAC) scale, Courtauld Emotional Control Scale (CECS), and the Duke–University of North Carolina Functional Social Support (DUFSS) questionnaire.

The HADS is a 14-item, self-administered questionnaire specifically designed for patients with physical illness[14] and validated in patients with cancer.[15] The item scores range from 0 to 3 and are summed so that the anxiety and depression subscales each range from 0 to 21. Scores greater than 10 indicate probable psychological morbidity, whereas scores between 7 and 10 indicate possible psychological morbidity. The HADS has been used in several breast cancer studies and has been shown to have a stable factor structure and high reliability (Cronbach's $\alpha > 0.9$ for both scales).[16]

The MAC scale was developed on the basis of extensive qualitative work identifying common responses to cancer and was designed to assess adjustment responses to cancer.[17] It has 40 items and five subscales, including fighting spirit, helplessness or hopelessness, anxious preoccupation, fatalism, and avoidance. The scales assess the extent to which these responses are adopted in the adjustment to the diagnosis and treatment of cancer. The internal consistency of the subscales is generally high, with α coefficients ranging from 0.65 (fatalism) to 0.84 (fighting spirit).[18]

The CECS is a 21-item questionnaire developed to measure the extent to which individuals report that they suppress emotions of anger, anxiety, and depressed mood. Subscales are consistent with these primary emotions: anger, depressed mood, and anxiety. Internal consistency is high, with α coefficients ranging from 0.86 (anger subscale) to 0.88 (depressed mood and anxiety subscales). One-month test-retest reliability for the total CECS is also high, with an α coefficient of 0.95.[19]

The DUFSS questionnaire is an eight-item measure that assesses self-perceived affective support and support from a confidant.[20] Affective social support covers support from people who care and from people who give love and affection. Confidant social support covers opportunities to talk about personal, financial, or work-related problems and invitations to participate in activities with others. The DUFSS has been validated in a primary care setting[21] and is regarded as a suitable measure for studying social support of patients with cancer.[22-24]

Medical history. Tumor characteristics, including size, grade, number of involved axillary nodes, and estrogen and progesterone receptor status, were obtained by central pathology review for 55% of cases. For the remainder, the information was abstracted from diagnostic pathology reports by trained research assistants. Other information abstracted from medical records included adjuvant therapy details (chemotherapy, hormonal therapy, duration, doses) and details of first distant recurrence and death.

Statistical Methods

Hazard ratios (HR) for DDFS and OS associated with psychosocial factors were estimated separately using Cox proportional hazards survival models, with and without adjustment for one or more of the following factors: number of involved axillary nodes (zero, one to three, four or more, unknown), tumor size ($\leq$ 20 mm, 21 to 50 mm, $>$ 50 mm, unknown), tumor grade (1, 2, 3, unknown), estrogen receptor status (negative, positive, unknown), progesterone receptor status (negative, positive, unknown), age at diagnosis in years ($<$ 35, 35 to 39, 40 to 49, 50 to 59 years), adjuvant systemic treatment (none, chemotherapy alone, tamoxifen alone, chemotherapy and tamoxifen, unknown), body mass index ($\leq$ 30 kg/m^2, $>$ 30 kg/m^2, unknown),[25] and time in years to diagnosis from last full-term pregnancy (nulliparous, $<$ 2, 2 to 4.99, $\geq$ 5 years).[26] Each psychosocial factor was analyzed as a categoric and a continuous variable. For the factors derived from the MAC scale and HADS, predetermined cutoffs were used,[15,18] and all others were dichotomized at the observed median.

The primary end point was DDFS, with time to distant recurrence (abstracted from medical records) measured from the date of diagnosis. Women who were not known to have had a distant recurrence, but died, were assumed to have had a distant recurrence at the date of death. All other women were censored at the date last known to be alive (ie, date of last contact with ABCFS study staff or date of last medical follow-up as abstracted from the medical records).

For the analysis of OS, time to death was considered from the date of diagnosis, with patients left-truncated at the date of interview. Women who were not known to have died were censored at the date last known to be alive.

Associations between psychosocial factors and tumor characteristics were assessed using unconditional logistic regression. Post hoc power calculations were conducted, assuming distant recurrence for 30% of patients over the observed follow-up period. All statistical analyses were performed using STATA version 9.0 (STATA Corp, College Station, TX), and all tests and *P* values were two-tailed.

RESULTS

Of the 797 Melbourne-based women in the ABCFS who were asked to complete a psychosocial questionnaire, 748 women (94%) did so. Of these, 40 patients were excluded for the following reasons: prior invasive (nonbreast) cancer (n = 23), older than 60 years at diagnosis (n = 8), metastatic disease at diagnosis (n = 5), and information on vital status after interview unavailable (n = 4). An additional 70 patients were excluded from the analyses for DDFS because consent to access information from medical records was not obtained and the occurrence of a distant recurrence could therefore not be determined. Thus there were 708 and 638 women included in the analyses for OS and DDFS, respectively.

The mean age at diagnosis of patients included in the analysis of DDFS was 40 years (standard deviation = 8.2 years). Median follow-up was 8.2 years (range, 0.8 to 14.4 years). Distant recurrence occurred in 209 (33%) of 638 patients, and 170 (24%) of 708 patients

died during the follow-up period. As shown in Table 1, 55% of patients had node-negative disease. Most (65%) had received adjuvant chemotherapy, 31% had received adjuvant hormonal therapy, and 18% had received no adjuvant treatment.

The distribution of scores for each psychosocial factor is summarized in Table 2. The prevalence of probable morbidity (HADS score > 10) was 3% for depression and 23% for anxiety. The prevalence of high fatalism was 5%.

There were no statistically significant associations between any of the measured psychosocial factors and DDFS or OS from the adjusted analyses (Table 3). From the unadjusted analysis, there was a marginally significant ($P = .02$) association between high scores on the MAC subscale for anxious preoccupation and poorer DDFS and OS (Table 3). This was only seen when it was analyzed as a continuous rather than dichotomous variable, and the association was no longer evident from the adjusted analysis. Allowing the association of anxious preoccupation on outcome to depend on the time delay between diagnosis and questionnaire administration showed that there was no association of delay with death ($P = .7$), but there was a tendency for the association with distant recurrence to be weaker if the data were collected further from diagnosis, although this was of marginal

Table 1. Patient Characteristics

Characteristic	No.	%
Age at diagnosis, years		
< 35	114	18
35-39	194	30
40-49	190	30
50-59	140	22
Body mass index, kg/m^2		
≤ 30	564	88
> 30	69	11
Unknown	5	1
Time to diagnosis from last childbirth, years		
Nulliparous	140	22
< 2	52	8
2-4.99	79	12
≥ 5	367	58
Tumor size, mm		
≤ 20	417	65
21-50	162	25
> 50	17	3
Unknown	42	7
Tumor grade		
1	80	13
2	244	38
3	260	41
Unknown	54	8
No. of involved axillary nodes		
0	348	55
1-3	166	26
> 3	88	14
Unknown	36	6
Estrogen receptor status		
Negative	263	41
Positive	350	55
Unknown	25	4
Progesterone receptor status		
Negative	229	36
Positive	384	60
Unknown	25	4
Systemic treatment		
Chemotherapy	416	65
Tamoxifen	200	31
Both	132	21
Neither	116	18
Unknown	38	6

Table 2. Prevalence of Psychosocial Factors (n = 638)

Factor and Instrument	Mean	SD	No.	%
Anxiety, HADS	7.5	4.3		
0-7			350	55
8-10			139	22
> 10			149	23
Depression, HADS	3.3	3.1		
0-7			565	89
8-10			56	9
> 10			17	3
Fighting spirit, MAC	52.5	5.9		
> 47			492	77
≤ 47			140	22
Unknown			6	1
Helplessness/hopelessness, MAC	10.5	2.3		
< 12			456	71
≥ 12			176	28
Unknown			6	1
Anxious preoccupation, MAC	23.2	3.7		
< 26			457	72
≥ 26			175	27
Unknown			6	1
Fatalism, MAC	16.1	3.8		
< 23			597	94
≥ 23			33	5
Unknown			8	1
Avoidance, MAC	1.7	0.8		
1-3			604	95
4			25	4
Unknown			9	1
Confidant support, DUFSS	20.4	4.0		
< 22			365	57
≥ 22			269	42
Unknown			4	1
Affective support, DUFSS	12.9	2.4		
< 15			407	64
≥ 15			224	35
Unknown			7	1
Anger control, CECS	15.1	4.5		
< 16			378	59
≥ 16			241	38
Unknown			19	3
Anxiety control, CECS	16.0	4.5		
< 17			333	52
≥ 17			289	45
Unknown			16	3
Depression control, CECS	16.1	4.7		
< 16			313	49
≥ 16			307	48
Unknown			18	3

Abbreviations: SD, standard deviation; HADS, Hospital Anxiety and Depression Scale; MAC, Mental Adjustment to Cancer; CECS, Courtauld Emotional Control Scale; DUFSS, Duke–University of North Carolina Functional Social Support.

Table 3. Psychosocial Measures and Distant Disease-Free and Overall Survival

	Distant Disease-Free Survival									Overall Survival								
	Recurrences			Crude			Adjusted*			Deaths			Crude			Adjusted*		
Factor	No. of Recurrences	Total Patients	%	HR	95% CI	P	HR	95% CI	P	No. of Deaths	Total Patients	%	HR	95% CI	P	HR	95% CI	P
Anxiety																		
0-7	114	350	33	1.00			1.00			98	394	25	1.00			1.00		
8-10	41	139	30	0.94	0.65 to 1.34	.7	1.03	0.71 to 1.50	.9	31	154	20	0.84	0.56 to 1.25	.4	0.80	0.52 to 1.21	.3
> 10	54	149	36	1.11	0.80 to 1.54	.5	0.96	0.67 to 1.36	.8	41	160	26	1.05	0.73 to 1.52	.8	1.00	0.68 to 1.47	.9
Continuous				1.00	0.97 to 1.03	.9	0.99	0.95 to 1.02	.4				1.00	0.97 to 1.04	.9	1.00	0.96 to 1.04	.9
Depression†																		
0-7	182	565	32	1.00			1.00			150	626	24	1.00			1.00		
8-10	19	56	34	1.15	0.72 to 1.85	.6	0.82	0.49 to 1.38	.5	14	62	22	0.97	0.56 to 1.68	.9	0.82	0.46 to 1.48	.5
> 10	8	17	47	1.39	0.69 to 2.84	.4	1.48	0.70 to 3.15	.3	6	20	30	1.23	0.55 to 2.79	.6	0.82	0.33 to 2.02	.7
Continuous				1.02	0.98 to 1.07	.3	1.00	0.96 to 1.05	.9				1.02	0.97 to 1.07	.5	0.99	0.94 to 1.04	.6
Fighting spirit																		
> 47	167	492	34	1.00			1.00			135	547	25	1.00			1.00		
≤ 47	41	140	29	0.86	0.61 to 1.21	.4	0.80	0.55 to 1.14	.2	35	154	23	0.90	0.62 to 1.30	.6	0.86	0.58 to 1.27	.5
Continuous				1.01	0.98 to 1.03	.7	1.01	0.98 to 1.03	.6				1.01	0.98 to 1.03	.06	1.00	0.98 to 1.03	.8
Helplessness																		
< 12	149	456	33	1.00			1.00			121	506	24	1.00			1.00		
≥ 12	59	176	34	1.03	0.76 to 1.39	.9	0.98	0.71 to 1.35	.9	49	195	25	1.08	0.77 to 1.50	.7	1.07	0.75 to 1.52	.7
Continuous				1.02	0.97 to 1.09	.4	1.01	0.95 to 1.07	.9				1.04	0.98 to 1.10	.2	1.04	0.97 to 1.11	.2
Anxious preoccupation																		
< 26	144	457	32	1.00			1.00			116	505	23	1.00			1.00		
≥ 26	64	175	37	1.26	0.94 to 1.69	.1	0.96	0.70 to 1.32	.8	54	196	27	1.26	0.911.74	.2	1.21	0.86 to 1.69	.3
Continuous				1.04	1.01 to 1.08	.02	1.01	0.97 to 1.05	.7				1.05	1.01 to 1.09	.02	1.03	0.99 to 1.07	.2
Fatalism																		
< 23	194	597	33	1.00			1.00			157	659	24	1.00			1.00		
≥ 23	13	33	39	1.43	0.81 to 2.51	.2	1.28	0.70 to 2.32	.4	12	40	29	1.36	0.76 to 2.45	.3	1.57	0.84 to 2.93	.2
Continuous				1.00	0.96 to 1.03	.9	1.01	0.97 to 1.05	.6				0.99	0.95 to 1.03	.5	1.00	0.95 to 1.04	.8
Avoidance																		
1-3	199	604	33	1.00			1.00			163	666	24	1.00			1.00		
4	8	25	32	0.92	0.45 to 1.86	.8	1.12	0.54 to 2.33	.8	6	31	19	0.74	0.33 to 1.68	.5	0.44	0.18 to 1.08	.07
Continuous				0.94	0.80 to 1.11	.5	1.05	0.88 to 1.26	.6				0.86	0.71 to 1.04	.1	0.88	0.72 to 1.06	.2
Confidant support																		
< 22	129	365	35	1.00			1.00			98	406	24	1.00			1.00		
≥ 22	80	269	30	0.90	0.68 to 1.19	.5	0.95	0.71 to 1.28	.8	72	298	24	1.00	0.74 to 1.36	.9	0.93	0.68 to 1.28	.7
Continuous				0.99	0.96 to 1.02	.6	0.99	0.96 to 1.03	.6				1.00	0.97 to 1.04	.9	1.00	0.97 to 1.04	.9
Affective support																		
< 15	139	407	34	1.00			1.00			112	455	25	1.00			1.00		
≥ 15	69	224	31	0.92	0.69 to 1.23	.6	1.02	0.75 to 1.38	.9	57	245	23	0.93	0.67 to 1.28	.6	0.87	0.62 to 1.21	.4
Continuous				1.01	0.96 to 1.07	.6	1.02	0.96 to 1.08	.6				1.03	0.97 to 1.10	.4	1.03	0.96 to 1.09	.4
Anger control																		
< 16	131	378	35	1.00			1.00			109	413	27	1.00			1.00		
≥ 16	72	241	30	0.83	0.63 to 1.11	.2	0.88	0.65 to 1.22	.3	56	274	20	0.75	0.54 to 1.04	.08	0.85	0.60 to 1.20	.4
Continuous				0.97	0.94 to 1.00	.07	0.98	0.94 to 1.02	.3				0.97	0.93 to 1.00	.08	0.98	0.95 to 1.02	.4
Anxiety control																		
< 17	111	333	33	1.00			1.00			90	367	25	1.00			1.00		
≥ 17	92	289	32	0.97	0.73 to 1.27	.8	0.19	0.89 to 1.59	.2	75	323	23	0.94	0.69 to 1.28	.7	1.10	0.80 to 1.51	.6
Continuous				0.99	0.96 to 1.02	.6	1.01	0.98 to 1.05	.5				0.99	0.96 to 1.03	.7	1.00	0.97 to 1.04	.8
Depression control																		
< 16	108	313	35	1.00			1.00			86	345	25	1.00			1.00		
≥ 16	95	307	31	0.88	0.67 to 1.16	.4	0.91	0.68 to 1.22	.5	79	343	23	0.89	0.66 to 1.21	.5	0.99	0.72 to 1.36	.9
Continuous				0.98	0.95 to 1.01	.2	0.99	0.96 to 1.03	.7				0.99	0.96 to 1.02	.5	1.00	0.96 to 1.03	.9

Abbreviation: HR, hazard ratio.

*Analyses adjusted for grade (1, 2, 3, unknown), estrogen receptor status (negative, positive, unknown), progesterone receptor status (negative, positive, unknown), size (≤ 20, 21-50, > 50 mm, unknown), number of involved nodes (0, one to three, four or more, unknown), body mass index (obese, not, unknown), time to diagnosis from last childbirth (nulliparous, < 2 years, 2 to <5 years, 5+ years), systemic treatment (chemotherapy only, tamoxifen only, chemotherapy and tamoxifen, neither, unknown).

†Results were not substantially changed when depression dichotomized at cut point of 8 (data not shown).

statistical significance ($P = .08$). For both outcomes, allowing for an influence of delay made no difference to the statistical significance of the associations with anxious preoccupation. Removing anxious preoccupation from the multivariate model made no substantive difference to the HR estimates for the covariates considered (data not shown). Higher scores for anxious preoccupation were associated with younger age at diagnosis ($P = .03$), higher tumor grade ($P = .02$), and greater number of involved axillary nodes ($P = .008$).

Because the prevalence of probable depression (HADS score of > 10) was low (3%), we repeated the analysis, dichotomizing the HADS score at a cut point of 8 (possible or probable depression *v* depression unlikely), and the results did not change substantially (data not shown).

Post hoc calculations indicated that this study had 80% power to detect relative risks of 2.0 or more for dichotomized factors with low prevalence (such as depression and fatalism) and relative risks of 1.5 or more for other more prevalent factors, such as anxiety.

DISCUSSION

From this large, population-based study, no statistically significant associations were found between psychosocial factors (measured at a median of 11 months after breast cancer diagnosis) and either DDFS or OS when adjusted for known prognostic factors. The observed association from the unadjusted analysis of high scores on the MAC subscale for anxious preoccupation was lost after adjustment for other known prognostic factors. The estimated effects of these established prognostic factors were not influenced by the inclusion of anxious preoccupation in the multivariate model. This suggests that the association of anxious preoccupation with outcome was due to its correlation with poor prognostic factors rather than it directly causing poorer outcomes. That is, younger women with poorer prognosis tumors, in terms of grade and axillary nodal status, were more likely to score high for anxious preoccupation, suggesting that the apparent influence of anxious preoccupation was mediated by these other well-established prognostic factors and their associated treatments (eg, chemotherapy), rather than being independently important.

A strength of this study was its relatively large sample size and length of follow-up, providing adequate statistical power to detect modest relative risks, even for uncommon factors such as depression. Another major strength of our study is that it was population-based, and thus the results are likely to be generalizable to women with disease in the relatively young age ranges studied. The focus on young women is appropriate because, as a group, they have more emotional distress than older women after a breast cancer diagnosis.[27] Also, we were able to adjust for a comprehensive range of potentially important prognostic factors, including tumor characteristics, treatment, and host factors (such as age, body mass index, and recency of childbirth).[25,26]

A potential limitation of our study was the lack of repeated evaluations of the psychosocial factors over time. These factors are dynamic, and previous studies have shown that psychosocial distress is most prevalent in the first few months after diagnosis and then, for the majority of women, returns to premorbid levels after approximately 1 year. We are unable to directly determine from our data whether women who had sustained, rather than transient, psychosocial distress might have been more likely to have worse survival. However, the fact that our questionnaires were not administered at a specific time point after diagnosis but rather over a range of time points (2 to 42 months) could be seen as at least partially mitigating this limitation because we found that adjusting for time between diagnosis and administration of the psychosocial questionnaires produced no substantive changes in the estimates for the association between anxious preoccupation and survival.

Comparison of the current study with much of the literature is difficult because of differences in study design such as study sample characteristics and the timing of measurement of psychosocial factors. Also, because of the wide range of psychosocial measures used in previous studies, even closely related terms derived from different instruments do not necessarily measure the same thing. Two relatively large recent studies used at least some of the same questionnaires as the current study.[28,29] A multivariate analysis of one of these, from the Danish Breast Cancer Cooperative Group, also failed to find any association between anxiety and depression (assessed by the HADS 2 months after diagnosis) and survival.[28] The other study examined the influence of psychological responses on breast cancer survival using a hospital-based cohort of 578 patients with initially 5 and later 10 years of follow-up.[29,30] At 5 years of follow-up, that study found worse overall survival from the adjusted analysis for women who had probable depression (HADS score > 10), with an HR of 3.59 (95% CI, 1.39 to 9.24; $P < .01$) and worse event-free survival of women with high (> 12) rather than low scores on the helplessness/hopelessness subscale of the MAC scale (HR = 1.55; 95% CI, 1.07 to 2.25; $P < .01$).[29] The effect of helplessness/hopelessness was sustained at 10 years of follow-up, but the effect of depression was no longer statistically significant: the authors concluded that "there has been no clear effect of depression on survival as assessed here."[30] In the current study, no association between depression or helplessness/hopelessness and breast cancer outcomes was observed, suggesting that neither of these factors substantially influence breast cancer survival.

Other large studies have not collected the same measures as our study. Hjerl et al, [31] using a retrospective study design, assessed the influence of affective disorders, defined as those necessitating psychiatric hospital admission. They reported that having an affective disorder after diagnosis of early-stage breast cancer was associated with increased mortality. Reynolds et al[32] examined coping strategies and breast cancer survival but found no significant associations for women with early-stage breast cancer. Kroenke et al[33] studied women with breast cancer in the Nurses Health Study. They showed that socially isolated women had an elevated risk of death owing to breast cancer and all causes, even after adjustment for multiple covariates, although the possibility of residual confounding by socioeconomic status could not be excluded. Tumor stage was adjusted for in the analysis, but early-stage patients and those with metastatic disease at diagnosis were not analyzed separately. This is an important point, because differential effects between patients with nonmetastatic and metastatic disease have been reported by others.[32,34]

Interestingly, a recent randomized controlled trial of cognitive-existential group therapy designed to improve mood and mental attitude toward cancer in early-stage breast cancer patients did not result in survival benefits.[35] This is consistent with the findings of the current study, either because psychosocial factors do not influence survival or alternatively because their impact is so small that a much larger study would be required to show benefit or deficit.

The current study does not support the hypothesis that the measured psychosocial factors influence survival after breast cancer. Psychosocial factors were not associated with large increases in the relative risk of recurrence, although smaller increases in risk (relative risk < 2.0 for depression and fatalism and < 1.5 for the other factors) cannot be excluded on the basis of this study alone. This should be reassuring for women, particularly those who experience substantial levels of psychosocial distress after their diagnosis. It is important to

note that this does not negate the potential value of interventions that reduce psychosocial distress in women with breast cancer, as these seem to improve quality of life.[36,37]

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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